AN \( \alpha \)-CELL HORMONE OF THE ISLETS OF LANGERHANS*

Sirs:

A second hormone of the islets of Langerhans, elaborated by the \( \alpha \)-cells and acting antagonistically to insulin, has long been suggested by (a) the many reports in the early insulin literature of a preliminary hyperglycemic action of certain relatively crude preparations of insulin protein,\(^1\) (b) the more recently recognized histological appearance of the \( \alpha \)-cells, which exhibit the granulation characteristic of endocrine function, (c) the reduction of the hyperglycemia, the development of ketosis, and the fatal termination which follow removal of the pancreas in the alloxan-diabetic dog,\(^2\) and (d) clinical data in "diabetes mellitus" which cannot be reconciled with absolute hypoinsulinism.

In a search for active extracts of the suspected \( \alpha \)-cell hormone, we have examined the physiological properties of various pancreatic fractions in the course of separation of crystalline zinc insulin\(^3\) and have succeeded consistently in obtaining preparations which cause liver glycogenolysis \((in \, vivo \, and \, in \, vitro)\) and hyperglycemia.

The supernatant solution from the first isoelectric precipitation of insulin\(^2\) was concentrated 10-fold \textit{in vacuo} at room temperature and the insulin inactivated by boiling (20 minutes) at pH 9.5 to 9.7 (with rejection of the formed precipitate). The table shows the effect of intraperitoneal injection of the filtrate into intact fed rats (2 ml. (14 mg. of nitrogen) \textit{per} animal; each figure represents the average of seven animals (glycogen) or four animals (sugar); the controls were injected with 2 ml. of a 1 per cent solution of casein).

The observed maximum differences are statistically significant and the above pattern has been reproduced many times with different strains of rats and with different pancreas extracts. In efforts to purify the active

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material, comparable potency has been attained in preparations containing 2 mg. of nitrogen per rat dose. Stored without preservative at 4° and pH 9.5, crude extracts lose considerable activity in 8 to 10 days; purified preparations are more labile (1 to 5 days).

<table>
<thead>
<tr>
<th>Time after injection</th>
<th>Liver glycogen</th>
<th>Blood sugar</th>
</tr>
</thead>
<tbody>
<tr>
<td>min.</td>
<td>gm. per cent</td>
<td>mg. per cent</td>
</tr>
<tr>
<td>0</td>
<td>3.78</td>
<td>106</td>
</tr>
<tr>
<td>20</td>
<td>3.75</td>
<td>112</td>
</tr>
<tr>
<td>40</td>
<td>3.13</td>
<td>105</td>
</tr>
<tr>
<td>60</td>
<td>3.08</td>
<td>100</td>
</tr>
<tr>
<td>90</td>
<td>2.65</td>
<td>105</td>
</tr>
</tbody>
</table>

Incubation (37°; 1 hour) of active extract with rat liver slices (Ringer-phosphate medium) increases oxygen consumption and releases 20 to 30 per cent more glucose than untreated controls. Large doses fail to alter the blood pressure of the atropinized cat. Similarly prepared extracts of muscle or liver could not be shown to affect liver glycogen or blood sugar. These control observations tend to preclude non-specific action, or mediation through the adrenal or anterior pituitary.

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CORRECTION

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